

Listing of Claims:

Claim 1 (original): A combination which comprises (a) an aromatase inhibitor and (b) a bisphosphonate in which the active ingredients (a) and (b) are present in each case in free form or in the form of a pharmaceutically acceptable salt, for simultaneous, concurrent, separate or sequential use in the prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition.

Claim 2 (original): A method of treating a patient suffering from a disease or condition which responds to aromatase inhibition comprising administering to the patient an effective amount of a bisphosphonate and an effective amount of an aromatase inhibitor, especially with the proviso that the patient is not additionally treated with a chemotherapeutic agent.

Claim 3 (original): The method of claim 2 for the treatment of a proliferative disease.

Claims 4-8 (cancelled)

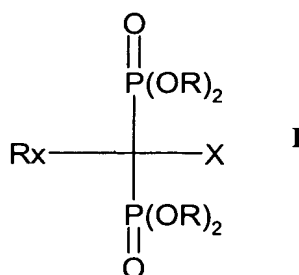
Claim 9 (original): A package comprising a bisphosphonate together with instructions for use in combination with an aromatase inhibitor for treatment of a disease or condition which responds to aromatase inhibition, especially with the proviso that the disease or condition is not additionally treated with a chemotherapeutic agent, or a package comprising an aromatase inhibitor together with instructions for use in combination with a bisphosphonate for treatment of a disease or condition which responds to aromatase inhibition, especially with the proviso that the disease or condition is not additionally treated with a chemotherapeutic agent.

Claim 10 (original): A package comprising a bisphosphonate together with instructions for use in combination with an aromatase inhibitor for prevention of bone loss which is caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition, or a package comprising an aromatase inhibitor together with instructions for use in combination with a bisphosphonate for prevention of bone loss which is caused by the

treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition.

Claim 11 (currently amended): The combination according to claim 1, ~~method according to claim 2 or 3, use according to any one of claims 4-8, or package according to claim 9 or 10,~~ in which the bisphosphonate is an N-bisphosphonate.

Claim 12 (currently amended): The combination, ~~method, use or package~~ according to claim 11 in which the bisphosphonate is a compound of formula I



wherein

X is hydrogen, hydroxyl, amino, alkanoyl, or an amino group substituted by C₁-C₄ alkyl, or alkanoyl;

R is hydrogen or C₁-C₄ alkyl and

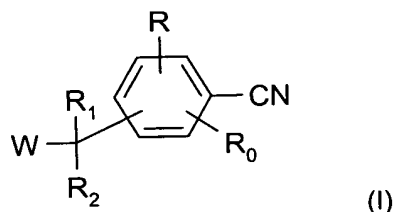
Rx is a side chain which contains an optionally substituted amino group, or a nitrogen containing heterocycle (including aromatic nitrogen-containing heterocycles), or a pharmaceutically acceptable salt thereof or any hydrate thereof.

Claim 13 (currently amended): The combination, ~~method, use or package~~ according to claim 12, in which the bisphosphonate is 2-(imidazol-1yl)-1-hydroxyethane-1,1-diphosphonic acid (zoledronic acid) or a pharmaceutically acceptable salt thereof.

Claim 14 (currently amended): The combination according to claim 1, ~~method according to claim 2 or 3, use according to any one of claims 4-8, or package according to claim 9 or 10,~~ in which the aromatase inhibitor is selected from exemestane, formestane, aminoglutethimide, vorozole, fadrozole, anastrozole, letrozole, roglethimide, pyridoglutethimide, trilostane, testolactone, atamestane, 1-methyl-1,4-androstadiene-3,17-dione, ketokonazole and pharmaceutically acceptable salts of these compounds.

Claim 15 (currently amended): The combination, ~~method, use or package~~ according to claim 14, in which the aromatase inhibitor is selected from exemestane, formestane, aminoglutethimide, fadrozole, anastrozole, letrozole and pharmaceutically acceptable salts of these compounds.

Claim 16 (currently amended): The combination according to claim 1, ~~method according to claim 2 or 3, use according to any one of claims 4-8, or package according to claim 9 or 10,~~ in which the aromatase inhibitor is a compound of formula I



wherein R and R₀, independently of one another, are each hydrogen or lower alkyl, or R and R₀ at adjacent carbon atoms, together with the benzene ring to which they are bonded, form a naphthalene or tetrahydronaphthalene ring; wherein R₁ is hydrogen, lower alkyl, aryl, aryl-lower alkyl or lower alkenyl; R₂ is hydrogen, lower alkyl, aryl, aryl-lower alkyl, (lower alkyl, aryl or aryl-lower alkyl)-thio or lower alkenyl, or wherein R₁ and R₂ together are lower alkylidene or C₄-C₆alkylene; wherein W is 1-imidazolyl, 1-(1,2,4 or 1,3,4)-triazolyl, 3-pyridyl or one of the mentioned heterocyclic radicals substituted by lower alkyl; and aryl within the context of the above definitions has the following meanings: phenyl that is unsubstituted or substituted by one or two substituents from the group lower alkyl, lower alkoxy, hydroxy, lower alkanoyloxy, nitro, amino, halogen, trifluoromethyl, cyano, carboxy, lower alkoxy carbonyl, carbamoyl, N-lower alkyl carbamoyl, N,N-di-lower alkyl carbamoyl, lower alkanoyl, benzoyl, lower alkylsulfonyl, sulfamoyl, N-lower alkylsulfamoyl and N,N-di-lower alkylsulfamoyl; also thienyl, indolyl, pyridyl or furyl, or one of the four last-mentioned heterocyclic radicals monosubstituted by lower alkyl, lower alkoxy, cyano or by halogen; or a pharmaceutically acceptable salt thereof.

Claim 17 (currently amended): The combination, ~~method, use or package~~ according to claim 16 in which the aromatase inhibitor is 4-[α-(4-cyanophenyl)-1-(1,2,4-triazolyl)methyl]--benzonitrile (letrozole) or a pharmaceutically acceptable salt thereof.

Claim 18 (original): A method of preventing bone loss in a patient suffering from an estrogen dependent disorder and receiving an aromatase inhibitor comprising administering to said patient an effective amount of a bisphosphonate.

Claim 19 (original): A method of preventing cancer treatment-related bone loss in a postmenopausal woman with ER+ and/or PR+ breast cancer receiving an aromatase inhibitor as adjuvant therapy comprising administering to said postmenopausal woman an effective amount of a bisphosphonate.

Claim 20 (currently amended): The method according to claim 18 ~~or 19~~ wherein the bisphosphonate is an N-bisphosphonate.

Claim 21 (original): The method according to claim 20 wherein the N-bisphosphonate is zoledronic acid or a pharmaceutically acceptable salt thereof.

Claim 22 (currently amended): The method according to ~~any one of claims 18-21~~ claim 18 wherein the aromatase inhibitor is letrozole or a pharmaceutically acceptable salt thereof.

Claim 23 (currently amended): The method according to ~~any one of claims 18-22~~ claim 18 wherein the bisphosphonate is administered once every six months.

Claim 24 (new): A method of treating or preventing bone loss caused by the treatment with an aromatase inhibitor of a disease or condition which responds to aromatase inhibition comprising administering to a patient in need of such treatment or prevention an effective amount of an aromatase inhibitor and an effective amount of a bisphosphonate.

Claim 25 (new): The method of claim 24 for the treatment of a proliferative disease.